UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,196	12/04/2001	Keith D. Allen	R-632	6896

7590 09/10/2003

DELTAGEN, INC.
740 Bay Road
Redwood City, CA 94063

EXAMINER
BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/10/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,196	ALLEN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,8-13 and 23-39* is/are pending in the application.

4a) Of the above claim(s) *1,2,11-13,24-28,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8-10,23,29-32 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Applicant's amendment filed on 06/23/2003 has been entered. Claims 3-5, 7, and 14-22 have been canceled. Claims 6,8-10,23, and 29-32 have been amended. Claims 35-39 have been added. Claims 1,2,6,8-13,23-39 are pending and claims 6,8-10,23, 29-32 and 35-39 are under consideration in the instant action.

Election/Restrictions

Claims 1,2,11-13,24-28,33 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Drawings

The drawings were received on 06/23/2003. These drawings are accepted.

Sequence Compliance

The instant application is now sequence compliant.

Specification

The specification was objected to because the sentence bridging lines 19-21 on page 1 was incomplete. This rejection was overcome by applicants' amendment replacing the paragraph with the first paragraph of page one of U.S. Provisional Application 60/311,056.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6,8-10,23, 29-32 and 35-39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are directed to a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits increased anxiety, decreased coordination or decreased susceptibility to seizure. The claims are further directed to cells isolated from the same mouse and method of screening agents that may modulate or ameliorate increased anxiety, decreased coordination or decreased susceptibility to seizure or, for some claims, ataxia, using the same mouse.

The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a G-protein coupled receptor. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype associated with a disruption of FPR-RS4. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ ID NO: 1. See page 21, last paragraph.

The specification has provided general assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice. As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be specific and substantial. The asserted utility does not appear specific and substantial to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between a homozygous disruption of the FPR-RS4 gene, increased anxiety, decreased coordination, decreased susceptibility to seizure or ataxia, and any disease or disorder. Since the evidence of record has not provided a correlation between increased anxiety, decreased coordination, decreased susceptibility to seizure or ataxia and any disease or disorder, the utility of identifying agents that affect increased anxiety, decreased coordination, decreased susceptibility to seizure or ataxia is not apparent. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and specific and substantial.

The instant specification has disclosed a transgenic mouse whose genome comprises a disruption in SEQ ID NO: 1, wherein the mouse exhibits increased anxiety, decreased coordination or decreased susceptibility to seizure or ataxia. See pages 55-57. The claims encompass said mouse, cells obtained from the mouse and methods of identifying agents that affect anxiety, balance, coordination or ataxia in the same mouse. The instant specification has discussed that the animals and cells of the instant invention can be used as models of disease (refer to pages 20-21). Specifically, the specification states that agents can be identified on the basis of their ability to affect at least one phenotype associated with a disruption of FPR-RS4

(page 21, lines 15-18). However, the evidence of record, while contemplating that the phenotypes inhibited by the claimed transgenic mice are associated with a disease, does not provide a correlation between the phenotypes of the claimed mouse and any disease or disorder. Furthermore, with respect to the phenotype of anxiety, Belzung (2001, Behavioral Brain Research, Vol. 125, pages 141-149) states that there are problems inherent in using knockout animals as models of anxiety as it is known that modulation of anxiety and other emotional disorders involves multiple genes and that this phenotype can be greatly influenced by genetic background. Belzung also states that responses exhibited by knockout mice considered to be animal models of anxiety may relate to behavioral process unrelated to anxiety. Belzung states further that knockout mice exhibiting anxiety are animal models of a single gene dysfunction rather than animal models of anxiety per se (Abstract, lines 8-10). Therefore, the reference suggests a need to provide independent evidence of an association of increased anxiety with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between increased anxiety or the other phenotypes displayed by the claimed mice and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be specific and substantial.

Claims 6,8-10,23, 29-32 and 35-39 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Upon overcoming the utility and enablement rejections set forth above, the following issues of enablement under 35 USC 112-1st paragraph must also be addressed.

1) The breadth of claims 6,8,9,10,23,29-32 and 35-39 is such that they encompass chimeric animals (genetic mosaics) wherein only a portion of the cells of the animal comprises the claimed genetic disruption. The specification teaches making transgenic animals whose genome comprises a homozygous disruption in the FPR-RS4 gene in all somatic and germ cells wherein the transgenic animals display increased anxiety, decreased coordination, decreased susceptibility to seizure and ataxia. The specification does not teach a chimeric animal with these phenotypes. The method of making genetic mosaic animals is such that each resulting chimera is comprised of a different, unpredictable ratio of cells of various genotypes. This ratio cannot be predetermined. Furthermore, the spatial distribution of cells of each genotype cannot be predetermined. Therefore, the phenotype of chimeric animals is not only dependent upon the genotype of the cells (which is unpredictable as set forth by the state of the art outlined on pages 9-11 of the previous office action mailed 12/18/2002; for example see Leonard; Moens;Griffiths, Mullins 1989,1990; Taurog) but is also dependent upon the spatial distribution of the cells and their relative population size. Thus, the phenotype of the chimeric animals encompassed by the claims is highly unpredictable. It would require undue experimentation for one of skill in the art to determine how to overcome the unpredictability associated with making chimeric animals

such that the proportion and population of cells harboring a genetic alteration could be controlled in such a way as to increase the predictability of the phenotype of the resulting chimeric animal.

2) The specification fails to enable the methods of claim 10. Claim 10 is directed to a method of using a mouse comprising a homozygous disruption in the FPR-RS4 gene to identify an agent that modulates expression or function of FPR-RS4. The specification teaches that a mouse comprising a homozygous disruption in the FPR-RS4 gene does not produce FPR-RS4. The specification does not teach what assay one of skill in the art would perform to determine the effect of an agent on a gene or gene product that is not present in the animal. If the gene or gene product is not present, it is not known how one would determine the effect of an agent on something that is not there.

3) Claim 30 is not enabled as written. Claim 30 uses the transgenic mouse of claim 6 which specifies that the mouse displays increased anxiety, decreased coordination and decreased susceptibility to seizure. Claim 6 does not list ataxia as a phenotype for the claimed mouse. However, dependent claim 30 includes the method step of determining whether an agent ameliorates ataxia in the mouse of claim 6. The specification does not teach how to determine whether an agent ameliorates ataxia in a mouse that does not exhibit ataxia and one of skill in the art would not know how to determine the effect of an agent on ataxia in a mouse that does not exhibit ataxia.

The rejection of claims 3-10,14-23 and 29-32 under 35 USC 112-1st paragraph for lacking enablement as set forth on pages 8-14 of the previous office action is withdrawn in view of Applicants' arguments.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 37 encompasses a transgenic mouse whose genome comprises a homozygous disruption in the FPR-RS4 gene wherein the mouse exhibits decreased coordination **wherein the decreased coordination is characterized by falling off the accelerating rotarod at a lower speed**. The specification teaches that the claimed mice fell off the rotarod after being on it a shorter time when compared to wildtype mice (page 57, lines 5-6). The specification provides no implicit or explicit support for the decreased coordination being characterized by falling of the accelerating rotarod at a lower speed encompassed by the bolded wherein clauses. The specification has only provided support for a decreased time to fall during the rotarod test. Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was

filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure* [or point to case law supporting incorporation of such a limitation as in the instant case]".

The rejection of claims 3-10,14-23 and 29-32 under 35 USC 112-1st paragraph for lacking written description as set forth on pages 7-8 of the previous office action is withdrawn in view of Applicants' arguments.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6,8,9,10,29-32 and 35-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6,9,10,23 refer to a homozygous disruption in FPR-RS4. As written, the term "FPR-RS4" can be interpreted as referring to the FPR-RS4 gene or the FPR-RS4 protein. A protein cannot have a homozygous disruption. Because the claim uses the phrase "homozygous disruption", the term "FPR-RS4 can be clarified by changing it to "the FPR-RS4 gene" in line 2

of claims 6,9,10 and 23 and in line 4 of claims 9 and 10 and in line 5 of claim 23. Claims 8, 29-32 and 35-39 depend from claim 6 and are included in this rejection.

Claim 9 is unclear because the language of the preamble is directed to a genetic mosaic as it states "...a transgenic mouse comprising a homozygous disruption..." However, step (d) of the claim encompasses breeding the chimeric mouse to generate transgenic mice whose genome comprises a homozygous disruption in the FPR-RS4 gene in all somatic and germ cells. Correction is required.

Claims 31 and 32 are unclear because the metes and bounds of the phrase "in vivo effects" cannot be determined. It is not clear from the claim or the specification what "in vivo effects" are encompassed by the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

PETER PARAS
PATENT EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632